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FILE 'HOME' ENTERED AT 15:44:22 ON 15 JUL 2003

=> file medline caplus biosis
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'MEDLINE' ENTERED AT 15:44:34 ON 15 JUL 2003

FILE 'CAPLUS' ENTERED AT 15:44:34 ON 15 JUL 2003
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FILE 'BIOSIS' ENTERED AT 15:44:34 ON 15 JUL 2003
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=> protease activated receptor
L1         1727 PROTEASE ACTIVATED RECEPTOR

=> broncho?
L2       168008 BRONCHO?

=> l1 and l2
L3           37 L1 AND L2

=> l3 and 1970-1999/py
L4            7 L3 AND 1970-1999/PY

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5            3 DUP REM L4 (4 DUPLICATES REMOVED)

=> d ti abs so l5 1-3

L5   ANSWER 1 OF 3     MEDLINE                          DUPLICATE 1
TI   A protective role for protease-activated
     receptors in the airways.
AB   The protection of cells in the upper intestine against digestion by
     pancreatic trypsin depends on the prostanoid prostaglandin E2 (PGE2) and
     is mediated by protease-activated receptors
     in the epithelium.  As the airway epithelium is morphologically similar
     and also expresses one of these receptors, PAR2, and is a major source of
     PGE2, we reasoned that bronchial epithelial PAR2 might also participate in
     prostanoid-dependent cytoprotection in the airways.  Here we show that
     activation of PAR2, which co-localizes immunohistochemically with
     trypsin(ogen) in airway epithelium, causes the relaxation of airway
     preparations from mouse, rat, guinea-pig and humans by the release of a
     cyclooxygenase product from the epithelium.  This physiological protective
     response in isolated airways also occurred in anaesthetized rats, where
     activation of PAR2 caused a marked and prolonged inhibition of
     bronchoconstriction.  After desensitization of PAR2, the response
     to trypsin recovered rapidly by mechanisms dependent on de novo synthesis
     and trafficking of proteins.  Our results indicate that trypsin released
     from the epithelium can initiate powerful bronchoprotection in
     the airways by activation of epithelial PAR2.
SO   NATURE, (1999 Mar 11) 398 (6723) 156-60.
     Journal code: 0410462. ISSN: 0028-0836.

L5   ANSWER 2 OF 3     MEDLINE                          DUPLICATE 2
TI   alpha-Thrombin stimulates contraction of human bronchial rings by
     activation of protease-activated receptors.
AB   In a variety of diseases, inflammation causes microvascular leakage and
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activates thrombin. Evidence suggests that thrombin increases cytosolic calcium and stimulates human airway smooth muscle (ASM) cell proliferation. The receptor subtypes, however, that mediate the effects of thrombin on ASM cell growth or calcium mobilization remain unknown. In this study, we postulate that thrombin, which activates specific **protease-activated receptors** (PARs), also stimulates contraction of isolated human bronchial rings. With the use of intact human bronchial rings, alpha-thrombin (1-20 U/ml) increased bronchial tone to 19 +/- 3% of basal tone (P = 0.008; n = 5 experiments) and represents 20 +/- 8% of the maximum carbachol response. The EC(50) for thrombin-induced force generation was 12.2 U/ml (95% confidence interval 9.9-15.3 U/ml) and was not altered in bronchial rings that had the epithelium removed. In parallel experiments, a specific thrombin receptor-activating peptide (TRAP-14; 0.1-100 micromol/l) increased isometric tension to levels (14 +/- 2%; P = 0.0005; n = 5 experiments) comparable to those rings stimulated with thrombin. To characterize the receptors that mediate thrombin effects on human ASM, the expression of PARs in cultured human ASM cells was analyzed by RT-PCR analysis with specific primers for PARs. In these cells, PAR1 (thrombin receptor), PAR2, and PAR3 were expressed at comparable levels. In other experiments using immunocytochemical staining with specific antibodies to PAR1 and PAR2, we showed that ASM in bronchial rings and cultured ASM cells express PAR1 and PAR2 proteins. Taken together, these studies suggest that alpha-thrombin, in a receptor-specific and dose-dependent manner, induces contraction of bronchial rings in vitro. In addition, cultured human ASM cells express mRNA of PAR1, PAR2, and PAR3 and express PAR1 and PAR2 protein. Further studies are needed to determine whether alpha-thrombin plays a role in stimulating **bronchoconstriction** in inflammatory airway diseases such as asthma and bronchiolitis obliterans.

SO AMERICAN JOURNAL OF PHYSIOLOGY, **(1999 Jul)** 277 (1 Pt 1) L22-9. Journal code: 0370511. ISSN: 0002-9513.

L5 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

TI A role for thrombin and proteinase-activated receptor 1 (PAR1) in guinea-pig **bronchospasm.**

SO British Journal of Pharmacology, (**Oct., 1997**) Vol. 122, No. PROC. SUPPL., pp. 14P.
Meeting Info.: Proceedings of the British Pharmacological Society Meeting Bristol, England, UK July 23-25, 1997 British Pharmacological Society . ISSN: 0007-1188.

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=> d au l5 1-3

L5   ANSWER 1 OF 3     MEDLINE                              DUPLICATE 1
AU   Cocks T M; Fong B; Chow J M; Anderson G P; Frauman A G; Goldie R G; Henry
     P J; Carr M J; Hamilton J R; Moffatt J D

L5   ANSWER 2 OF 3     MEDLINE                              DUPLICATE 2
AU   Hauck R W; Schulz C; Schomig A; Hoffman R K; Panettieri R A Jr

L5   ANSWER 3 OF 3  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AU   Cicala, C. (1); Bucci, M. (1); De Dominicis, G.; Cirino, G.


=> thomas?/au and cocks?/au
L6          20 THOMAS?/AU AND COCKS?/AU

=> james?/au and moffett?/au
L7           1 JAMES?/AU AND MOFFETT?/AU

=> d his

     (FILE 'HOME' ENTERED AT 15:44:22 ON 15 JUL 2003)
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     FILE 'MEDLINE, CAPLUS, BIOSIS' ENTERED AT 15:44:34 ON 15 JUL 2003
L1          1727 PROTEASE ACTIVATED RECEPTOR
L2        168008 BRONCHO?
L3            37 L1 AND L2
L4             7 L3 AND 1970-1999/PY
L5             3 DUP REM L4 (4 DUPLICATES REMOVED)
L6            20 THOMAS?/AU AND COCKS?/AU
L7             1 JAMES?/AU AND MOFFETT?/AU
L8             0 L6 AND L1
L9             0 L7 AND L1

=> logoff
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